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Case Report & Case Series

Metastatic neuroendocrine tumor with initial presentation of orbital apex syndrome

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ABSTRACT

The possible etiologies of orbital apex syndrome range from inflammatory, infectious, neoplastic, iatrogenic/traumatic, to vascular processes. In patients without obvious infection or systemic cancer history, judicious use of corticosteroids is a reasonable strategy. We describe a 64-year-old man who presented with orbital apex syndrome and had progressed to total visual loss in three days after admission. Radiological imaging and pathological studies were consistent with a neuroendocrine tumor with multiple metastases. We recommend that a biopsy-proven specimen is warranted in patient with orbital apex syndrome even without a cancer history.

1. Introduction

Lesions affecting the anatomically adjacent structures, including optic nerve (II), oculomotor nerve (III), trochlear nerve (IV), abducens nerve (VI), ophthalmic/maxillary branch of the trigeminal nerve (V1, V2) and oculosympathetic fibers, may cause three partially overlapping clinical syndromes: superior orbital fissure, orbital apex, and cavernous sinus syndrome. The etiologies causing these syndromes are also quite similar, i.e., inflammatory, infectious, neoplastic, iatrogenic/traumatic, or vascular processes. Based on the broad spectrum of etiologies, the decision on evaluation and management remains a great challenge to clinical physicians [1]. For example, the use of corticosteroids is warranted for inflammatory process, but may be harmful to some infection etiologies. Also, conservative measures may be adequate for some causes, whereas urgent procedures are necessary in others.

Possible primary tumors involving the orbital apex and cavernous sinus include lymphoma, neural tumors and local invasion from adjacent head and neck tumors. The metastatic tumors include the origins from breast, lung, kidney and malignant melanoma. Some inflammatory causes, like orbital pseudotumor, Tolosa-Hunt syndrome, and thyroid orbitopathy, may mimic neoplasms [1–3]. Among the neoplasms, neuroendocrine tumor is relatively rare and usually arises from gastrointestinal tract or bronchopulmonary source [4]. Here, we reported a rare case of high grade neuroendocrine tumor of unknown primary site with initial presentation of progressive ptosis and vision loss as orbital apex syndrome, which highlighted the importance of obtaining biopsy-proven specimen in such patients.

2. Case report

A 64-year-old man was previously healthy and was referred to neurological clinic for ptosis in the left eye. He had acute onset of ptosis, retro-orbital soreness and mild blurred vision on the left side for one month. There was no double vision and motor or sensory symptoms. There was also no fever, rhinorrhea, nose stuffy, and tinnitus. The orbital symptoms had progressed gradually without obvious diurnal change. Neurologic examinations showed left ptosis, mild palpebral swelling without erythematous change, sluggish light reflex and slight upper ward gaze limitation in the left eye. The visual acuity was 6/10 in the right eye and 6/12 in the left eye on the day of admission. The symptom had progressed rapidly within three days that there was no light perception and full dilated pupil without light reflex in his left eye. The laboratory tests for inflammation and infection, including complete blood count with differential count, erythrocyte sedimentation rate, C-reactive protein, were normal. The serologic studies, including liver and renal function, along with carcinoembryonic antigen and alpha-fetoprotein, were also normal. The acetylcholine receptor antibody was within normal range. The magnetic resonance imaging of brain revealed a prominent left cavernous sinus with increasing soft tissue component that anteriorly extended into the orbital cavity, and heterogeneous enhancement in the retrobulbar space. Trace enhancements in the intracavernous and retrobulbar spaces were also depicted (Fig.1). He underwent sphenoethomoidectomy, and a dark reddish tumor was found at the opticocarotid recess. The pathology of the tumor showed large polygonal cells with hyperchromatic nuclei, distinct nucleoli and moderate pink cytoplasm (Fig. 2), and immunoreactivity to several immunohistochemical stainings, including cytokeratin, neuron-specific enolase, synaptophysin and chromogranin A, which

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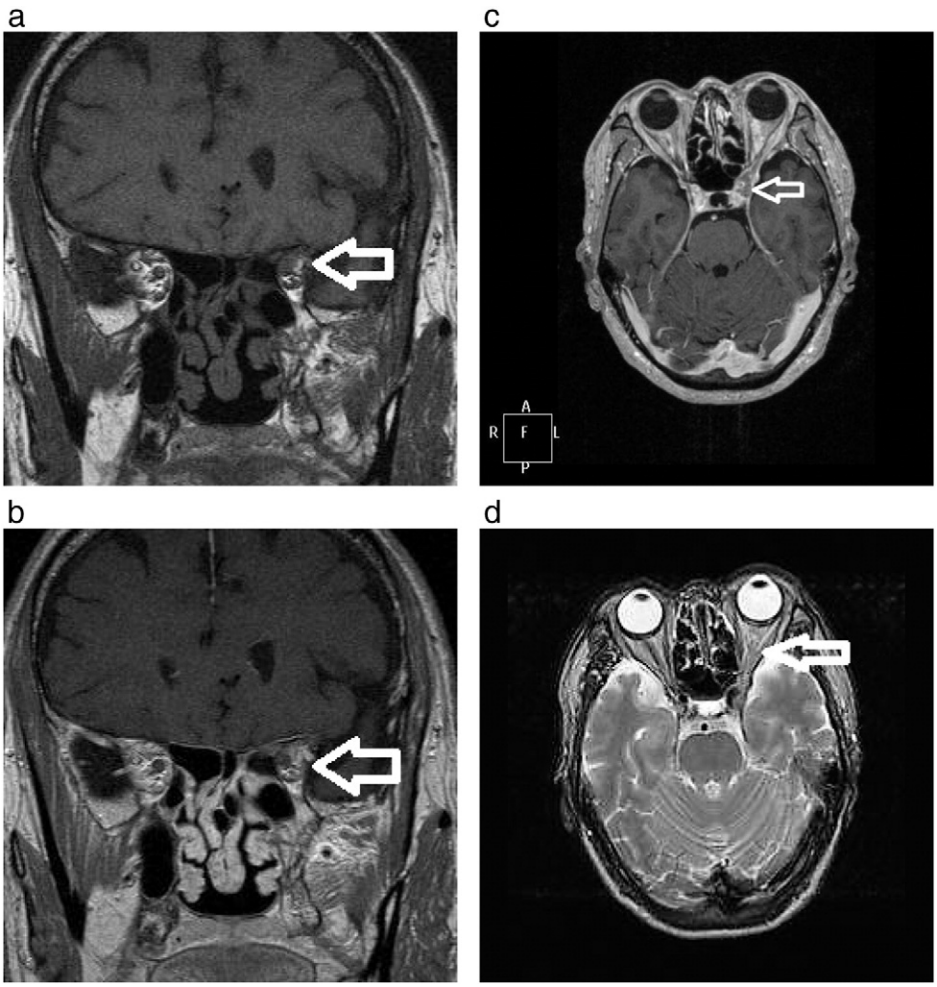

Fig. 1. Coronal contrast and noncontrast T1 weighted images (A, B), axial contrast T1 weighted image (C), and axial T2 weighted image (D). These pictures showed the heterogeneous soft tissues within the orbital apex, extending to orbital canal and cavernous sinus (arrows).

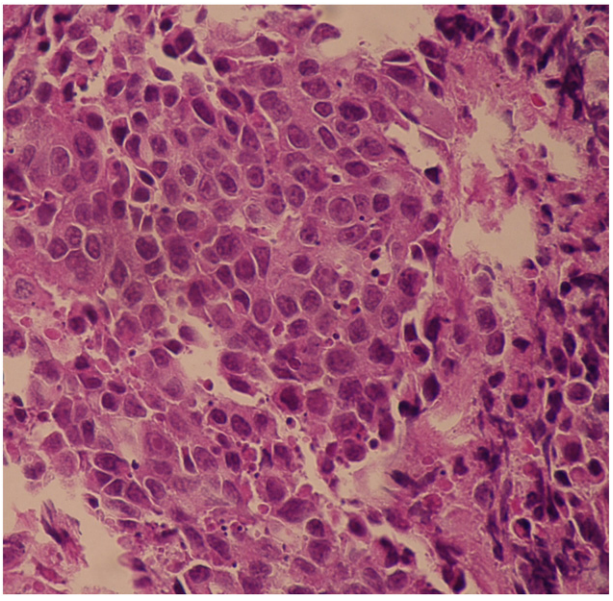

Fig. 2. The tumor tissue composed of large polygonal cells with hyperchromatic nuclei, distinct nucleoli and moderate pink cytoplasm (H&E stain, 400×).

were compatible with a neuroendocrine tumor. Positron emission tomography/computed tomography (PET/CT) scan showed increased multiple uptakes at the left orbital area, spines, rib cages and liver (Fig.3). Echo-guided liver biopsy revealed the same high grade malignant tumor with neuroendocrine differentiation. The primary site of the tumor was unclear. The patient died six months after initial symptoms.

3. Discussion

The orbital apex tumors range from benign inflammatory process to high grade malignancy. Ocular symptom is the initial manifestation of metastatic orbital tumors in up to 25% [5]. The diagnosis may be difficult in patients without history of systemic cancers. Neuroendocrine tumors are rare among the metastatic orbital tumors, and the clinical manifestation may masquerade cellulitis [2] or Graves orthopathy [3]. Furthermore, metastases are found in about 20% of the patients with neuroendocrine tumors at the time of diagnosis [6]. Similar to our patient but with a different scenario, a patient was reported previously with an unknown origin of neuroendocrine tumor in liver and was found to have orbital metastasis on both sides six month later [7].

When the cause of orbital apex is unable to be determined, possible management options include observation, an empirical trial of corticosteroid, and surgical biopsy. Because the distinctions among inflammation, infection, and neoplasm are often difficult and all may respond initially to corticosteroids, a short period of therapeutic corticosteroid

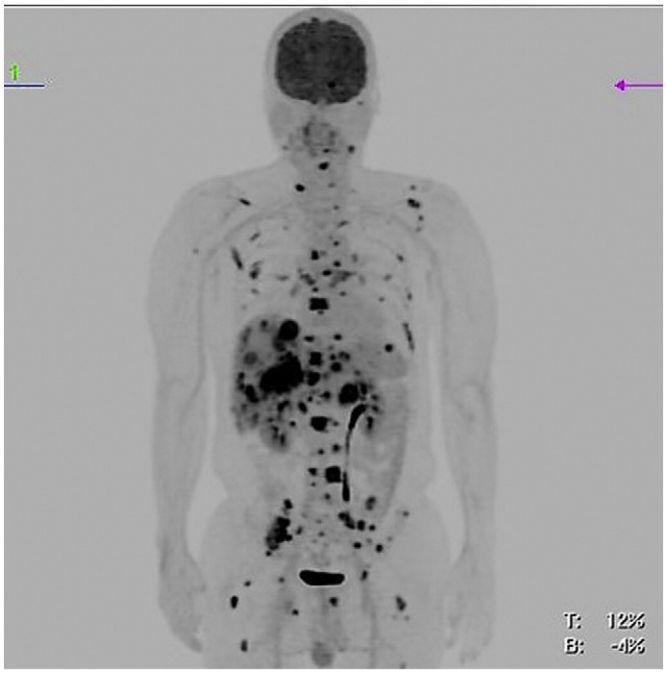

Fig. 3. Positron emission tomography with 2-deoxy-2-[fluorine-18] fluoro-D-glucose integrated with computed tomography (^{18}F-FDG PET/CT) showed intense uptake in left retro-orbital region and paranasal sinus. The intense uptake also involved the spine, rib cage, pelvic bones, bilateral femora and both lobes of liver.

trial has been suggested in the patients without systemic signs of infection or cancer history [1]. Because of the acute onset of symptoms with rapid progression that seemed to be more typical of an inflammatory process, a trial of corticosteroid was considered and used. After excluding the possibility of a vascular source by images and obtaining sufficient support of biopsy technique, a fine needle biopsy was considered at first. Because of rapidly loss of vision, however, sphenoethomoidectomy was done for the additional purpose of decompression. Without the tissue proof, the strategy of corticosteroid use may delay the diagnosis and further management in our patient.

From this experience, we recommend that a tissue proof may need to be considered first if the surgical risk is not high or the vision loss or ophthalmalgia is progressing rapidly. Pathological evidence is crucial for the diagnosis in patients with orbital apex syndrome, and an immunohistochemistry study may be helpful in identifying a neuroendocrine origin. When the neuroendocrine tumor is confirmed, further investigations of primary origin and possible systemic metastases are mandatory.

Conflicts of interest/disclosures

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

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